

**R E M A R K S**

Applicants acknowledge with appreciation the telephonic interview with the Examiner and Supervisor. The contents of the interview are discussed below in the context of the response. The Examiner provides a number of rejections and we list them here in the order in which they are addressed:

1. Claims 1, 13 and 15-16 were rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite.
2. Claims 1, 13 and 15-16 were rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Benning in view of Essigmann *et al.* and of Güler *et al.*

**I. THE CLAIMS ARE DEFINITE**

The Examiner rejected the claims under 35 U.S.C. § 112, second paragraph. The Examiner argued that "it is unclear how the peptides are reacted . . ." (Office Action, page 2). Applicants note in response that the specification, among other things, describes both biochemical reactions (outside of the cell) and transformation of host cells (whereupon the host cells express the enzymes and make products - such as sulfoquinovosyl diacylglycerol - in the cell). Each of these embodiments is discussed below.

**A. The In Vitro Embodiment**

Claims 1, 13 and 15-16 are directed to a biochemical reaction in vitro. While expression in host cells may take place prior to the steps in the claim (the claim is open-ended because of the term "comprising"), it is contemplated that the reactions take place outside the cell. While Applicants believe that the unamended claims are sufficiently definite, to further the prosecution (and without waiving the right to prosecute the unamended claims or similar claims in the future) Claims 1, 13 and 15-16 have been amended to indicate that the peptides are "isolated" prior to the biochemical reactions.<sup>1</sup> It is believed that these amendments overcome the rejection.

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<sup>1</sup> The other amended language is directed to the fact that SEQ ID NO:3 is a genomic sequence.

**B. The Co-expression Embodiment**

Claims 17-34 have been added. These claims are directed to embodiments wherein the peptides are co-expressed in a host cell and products are made by the host cell. The embodiments are described in the specification in various places, including but not limited to pages 42-46. It is believed that these claims are definite.

**II. THE CLAIMS ARE PATENTABLE OVER THE REFERENCES CITED**

The Examiner has rejected the claims under 35 U.S.C. 103(a) as being unpatentable over Benning in view of Essigmann *et al.* and Güler *et al.* It is respectfully submitted that the Examiner is reading too much into these references.<sup>2</sup> As discussed in telephonic interview, these references, while discussing possibilities and putative pathways, do not describe an in vitro assay for the generation of the products set forth in the claims. By contrast, the inventor and colleagues published in 2001 the first paper ever that describes the in vitro assay and the testing necessary to determine the sulfur donor (see Sanda *et al.* attached hereto at Tab A). The Examiner's attention is respectfully directed to page 3943 (left column header: "Confirmation of Sulfite as the Sulfur Donor") where it is noted:

"Thus far, the greatest mystery in the elucidation of the biosynthetic pathway for sulfolipid biosynthesis has been the nature of the sulfur donor for the formation of UDP-SQ. The establishment of the SQD1 in vitro assay described above gave us the opportunity to directly address this problem. . . . We therefore tested these compounds . . . to determine whether they could stimulate the formation of UDP-SQ. The addition of sulfate, APS, and PAPS had no effect . . . The addition of . . . thiosulfate, sulfide, and sulfogluthathione resulted . . . in an increase . . . We assumed that in all three instances, this effect was due to sulfite, . . . To corroborate this hypothesis, it was necessary to directly test the incorporation of labeled sulfite into UDP-SQ . . . When SQD1 was present in the APR1 reaction mixture, sulfite was converted . . . (Fig. 4, C and D). . . ."

It is clear from this publication that - until these experiments - the nature of the sulfur donor was a "mystery." Thus, the Examiner's contention that the cited references teach the sulfur donor is mistaken.

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<sup>2</sup> Applicants re-affirm their position that there is no basis for the combination of the references, that there is no showing of an expectation of success, and that even if (improperly combined) the references do not teach all the elements (see previous response for the details of these arguments).

As noted above, the new claims are directed to co-expression embodiments. The support in the specification for these embodiments was noted above. With respect to the non-obvious nature of these embodiments, the Examiner's attention is respectfully directed to the Yu *et al.* *PNAS* publication dated 2002 (attached hereto at Tab B) which describes - for the first time - the co-expression of SQD1 and SQD2 to produce sulfolipid in an organism that normally lacks it, namely *E. coli*. It is submitted that the patentability of these claims is evident.

### CONCLUSION

The Applicant believes that the arguments and claim amendments set forth above traverse the Examiner's rejections and, therefore, request that these grounds for rejection be withdrawn for the reasons set above. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, the Applicants' encourage the Examiner to call the undersigned collect at 617.252.3353.

Dated: \_\_\_\_\_

October 23, 2002

By: \_\_\_\_\_

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APPENDIX I

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1. (Twice Amended) A method, comprising:
  - a) providing:
    - i) uridine-5'-diphosphoglucose;
    - ii) sulfite;
    - iii) an isolated first peptide encoded by the nucleic acid sequence set forth in SEQ ID NO: 6; and
    - iv) an isolated second peptide encoded by a nucleic acid selected from the group consisting of SEQ ID NO:1 and the cDNA corresponding to SEQ ID NO:3;
  - b) reacting said uridine-5'-diphosphoglucose with said first peptide and said sulfite under such conditions that uridine-5'-diphosphosulfoquinovose is generated; and
  - c) treating said uridine-5'-diphosphosulfoquinovose with said second peptide under conditions such that sulfoquinovose diacylglycerol is generated.
  
13. (Twice Amended) A method, comprising:
  - a) providing:
    - i) uridine-5'-diphosphoglucose;
    - ii) sulfite; and
    - iii) an isolated peptide encoded by the nucleic acid sequence set forth in SEQ ID NO: 6; and
  - b) reacting said uridine-5'-diphosphoglucose with said peptide and said sulfur donor under such conditions that uridine-5'-diphosphosulfoquinovose is generated.

15. (Amended) A method, comprising:

- a) providing:
  - i) uridine-5'-diphosphoglucose;
  - ii) sulfite;
  - iii) the nucleic acid sequence set forth in SEQ ID NO: 6; and
  - iv) a host cell;
- b) transfecting said host cell with said nucleic acid under conditions such that a peptide is expressed; [and]
- c) isolating said expressed peptide; and
- [c]d) reacting uridine-5'-diphosphoglucose with said peptide of step (c) and said sulfite under conditions such that uridine-5'-diphosphosulfoquinovose is produced.

16. (Amended) A method, comprising:

- a) providing:
  - i) uridine-5'-diphosphosulfoquinovose;
  - ii) diacylglycerol;
  - iii) a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 and the cDNA corresponding to SEQ ID NO:3; and
  - iv) a host cell
- b) transfecting said host cell with said nucleic acid under conditions such that a peptide is expressed; [and]
- c) isolating said expressed peptide; and
- [c]d) reacting uridine-5'-diphosphosulfoquinovose with said peptide of step (c) and said diacylglycerol under conditions such that sulfoquinovosyl diacylglycerol produced.